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Case Report

Gaucher Disease in Men. A Clinical Case

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Abstract

A clinical case of a man with Gaucher disease type 1 (mental underdevelopment, hepatosplenomegaly, anemia, thrombocytopenia) and the threat of rupture of the spleen is presented. The disease has been manifested since childhood. The diagnosis was made on the basis of the clinic, medical history, life, objective data and instrumental research methods. As well as a decrease in the activity of acidic β-glucocerebrosidase in blood leukocytes and a mutation on the long arm of chromosome 1 (region 1q21q31).

Keywords: Gaucher Disease; Clinical Case; The Threat of Rupture of the Spleen; Male

Abbreviations

AC: Abdominal Cavity; ALP: Alkaline Phosphotase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BA: Blood Amylase; Bas: Basophils; BBT: Biochemical Blood Test; BI: Blood Iron; BMI: Body Mass Index; CCH: City Clinical Hospital; Ceg: Segmental; EAH: Electrical Axis of the Heart; ECG: Electrocardiography; Ery: Erythrocytes; FGDS: Fibrogastroduodenoscopy; Fib: Fibrinogen; FRM: Frequency of Respiratory Movements; FSBEI FPE RMACPE MOH : Federal State Budgetary Educational Institution of Further Professional Education "Russian Medical Academy of Continuing Professional Education of the Ministry of Healthcare; GBT: General Blood Test; GGTP: Gamma-Glutamyltranspeptidase; Hemg: Hemoglobin; KSMA: Kazan State Medical Academy; Leu: Leukocytes; LV: Left Ventricle; Lym: Lymphocytes; Mon: Monocytes; Pal: Palochki; Pl: Platelets; PTI: Prothrombin Index; RES: Rate of Erythrocyte Sedimentation; UDCA: Ursodeoxycholic Acid; USE: Ultrasound Examination; VVE: Varicose Veins of the Esophagus

Patient B., 36 years old, was admitted on 02.02.2019 to the therapeutic department of the City Clinical Hospital (CCH) No. 12 at Kazan city for urgent indications, 3 days after the onset of the disease. Complaints: chest pain on the left, cough with a small amount of yellow sputum, general weakness, difficulty breathing.

Anamnesis of the disease

Considers himself ill for a month. He became acutely ill on January 9, 2019 - there was pain in the left half of the chest, unrelated to the act of breathing, weakness and an increase in body temperature to 39^{0}C. On January 10, 2019, for urgent indications, he was admitted to inpatient treatment at CCH No. XXX at Kazan city. There was diagnosed with community-acquired left-sided pneumonia complicated by pleurisy. He was discharged for outpatient treatment on 25.01.2019. For 5 days, he took levofloxacin 500 mg x2 times a day and ambroxol 30 mg 2 times a day. The temperature dropped to 37.5^{0}C. From 01.02.2019 the condition worsened - the temperature rose to 39^{0}C, the cough intensified, pain appeared in the left half of the abdomen. An ambulance was called, taken to CCH No. 12, examined by a surgeon, no data for acute surgical pathology was revealed. An X-ray of the chest organs shows infiltration of lung tissue in the lower lobe of the left lung.

Anamnesis of life

Not married. Does not work. There is one in the family. Father is 61 years old, mother is 58 years old, alive and well (parents divorced 32 years ago.) Allergic history and drug intolerance: chlorine in the form of itchy skin. He denies infectious hepatitis, sexually transmitted diseases, and tuberculosis. There were no blood

transfusions. Heredity is not burdened. Transferred illness: has been registered with a psychiatrist since 1986. For a long time, liver damage was diagnosed (hepatitis, then cirrhosis of the liver), ursodeoxycholic acid (UDCA) drugs were prescribed. He denies bad habits. He did not serve in the army (a disabled person of the 2nd group for mental illness).

Objective present state

Height 160 cm, weight 52 kg., body mass index (BMI) = 20.3 kg/m^2. The condition is of moderate severity, consciousness is clear. He does not answer questions immediately, is somewhat inhibited, and is not always adequate due to mental retardation. The skin and visible mucous membranes are pale in color. Peripheral lymph nodes are not enlarged, there are no edema. Musculoskeletal system: kyphoscoliosis.

- **Respiratory system:** From the bottom left, the percussion sound above the pulmonary fields is somewhat shortened. There are also auscultatively small bubbly wheezes, frequency of respiratory movements (FRM) 20 per minute. SpO_2 - 97%.
- **Cardiovascular system:** Pulse and heart rate 126 beats per minute, satisfactory filling, blood pressure 110/60 mmHg. The boundaries of the heart are not expanded. The heart tones are muted, rhythmic.
- **Digestive system:** The tongue is overlaid with a whitish coating. The abdomen is sharply enlarged in volume due to pronounced hepatosplenomegaly (Figure 1). On palpation, it is painful in the left half of the abdomen. The liver according to M.G. Kurlov is 20x25 cm, the size of the left lobe cannot be determined due to an enlarged spleen. The spleen is the lower edge below the navel level.
- **The urinary system:** Without features, F.I. Pasternatsky's symptom (a symptom of pounding) is negative on both sides. Urination is painless, diuresis is normal.

The following laboratory and instrumental studies were carried out (normal indicators accepted at the clinic are indicated in parentheses).

General blood test (GBT) at 02.02.2019: erythrocytes (Ery): 3,28x10^{12}/L (4.0-5,1x10^{12}/L), hemoglobin (Hemg): 86 g/l (132-164 g/l), platelets (Pl): 81x10^9/L (180-320x10^9/l); leukocytes

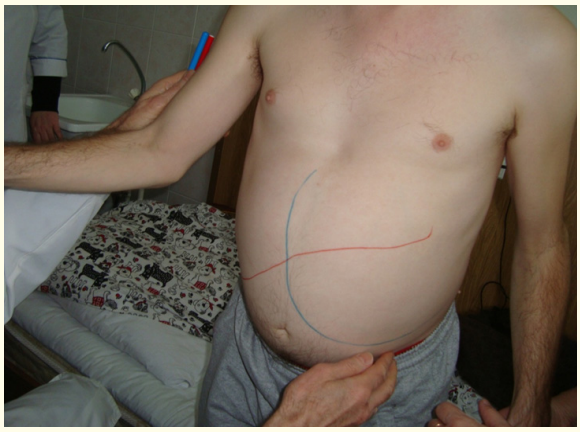

Figure 1: The contour of the liver is marked in red, the spleen in blue.

(Leu): 12,35x10^9/L (4.0-9.0x10^9/l, palochki (Pal): 2% (1-6%), segmental (Ceg): 78% (45-70%), lymphocytes (lym): 16% (18-43%), monocytes (Mon): 4% (2-9%), the rate of erythrocyte sedimentation (RES): 23 mm/h (2-15 mm/h).

GBT at 05.02.2019: Ery: 2,06x10^{12}/l, Hemg: 54 g/l, Pl: 158x10^9/l; Leu: 11,40x10^9/l, basophils (Bas): 1%, Pal: 4%, Ceg: 81%, Lym: 13%, Mon: 2%, RES: 20 mm/h.

GBT at 06.02.2019: ERy: 2,25x10^{12}/l, Hemg: 60 g/l, Pl: 190x10^9/l; Leu: 13,08x10^9/l, Bas: 1%, Pal: 4%, Ceg: 82%, lym: 8%, Mon: 2%, RES: 32 mm/h.

Biochemical blood test (BBT) from 02.02.2019: total bilirubin: 15.1mmol/l (8.5-20.5mmol/l), direct bilirubin: 4.7mmol/L (3.4mmol/L), indirect bilirubin: 10.4mmol/L (1.7-17.0mmol/L), alanine aminotransferase (ALT): 59ed/L (<40), aspartate aminotransferase (AST): 120ed/L (<40), blood amylase (BA): 30 u/L (<95), gamma-glutamyltranspeptidase (GGTP): 60ed/L (<50), alkaline phosphotase (ALP): 189.2 u/L (<120), prothrombin index (PTI): 71% (80-100), fibrinogen (Fib): 2.8 g/l (2-4), blood iron (BI): 7.7mmol/l (12.5-32.2).

BBT from 02.05.2019: total bilirubin: 16.4mmol/L (8.5-20.5mmol/L), ALT: 67ed/L (<40), AST: 128ed/L (<40), BA: 36ed/L (<95), GGTP: 74ed/L (<50), ALP: 201.8u/L (<120), PTI: 70% (80-100), Fib: 2.2 g/l (2-4), BI: 8.1mmol/l (12.5-32.2).

BBT from 02.06.2019: total bilirubin: 18.5 mmol/L (8.5-20.5mmol/L), ALT: 64ed/L (<40), AST: 132ed/L (<40), BA: 42ed/L (<95), GGTP: 67ed/L (<50), ALP: 222.3u/L (<120), PTI: 73% (80-100), Fib: 2.6 g/l (2-4), BI: 8.6mmol/l (12.5-32.2).

BBT from 09.02.2019: total bilirubin: 15.3mmol/L (8.5-20.5mmol/L), ALT: 42ed/L (<40), AST: 58ed/L (<40), BA: 37ed/L (<95), GGTP: 48ed/L (<50), ALP: 124.5u/L (<120), PTI: 76% (80-100), Fib: 2.6 g/l (2-4), BI: 8.2mmol/l (12.5-32.2).

Ultrasound examination (USE) of the abdominal cavity (AC) from 02.02.2019: liver: right lobe 148 mm (up to 140 mm), left lobe 76 mm (up to 70 mm), protrudes from under the edge of the costal arch by +4 cm. The contours are smooth. Echogenicity is moderately increased. The echostructure is homogeneous. Gallbladder: dimensions 74 x 23mm. The walls are normal. The contents are homogeneous. The holedoch is 5 mm (up to 5 mm). Pancreas: not visualized, blocked by the spleen and liver. Portal vein 11 mm (up to 12mm). Spleen: enlarged, size 184x97mm (110x50x50mm). The contours are uneven. The structure is diffusely heterogeneous. Free fluid: detected in the pelvis, a small amount.

USE of the hepatobiliary system from 02.06.2019: splenic vein 16 mm (up to 6 mm). Spleen: Dimensions: 232x108 mm (120x60 mm). The contours are smooth. The structure is heterogeneous due to iso-, hypoechoic formations up to 74x84 mm with uneven contours, heterogeneous structure. No free fluid was detected in the abdominal cavity.

USE of the pleural cavity from 02.02.2019: no free fluid is detected on the right. In the pleural cavity on the left, there is free fluid in the bone-diaphragmatic sinus in the form of a strip.

USE of the kidneys from 02.06.2019: Right kidney: 85x40 mm. The thickness of the parenchyma is 12 mm. The contours are clear. The location has not been changed. Mobility is preserved. The cup and tub system is not expanded. Hyperechoic structures: none. Left kidney: 96x42 mm. The thickness of the parenchyma is 13 mm. The contours are clear. The location has not been changed. Mobility is preserved. The cup and tub system is not expanded. Hyperechoic structures: none.

Fibrogastroduodenoscopy (FGDS) 02.02.2019: esophagus: we pass freely throughout, the mucous membrane is normal, the cardiac pulp closes completely. Stomach: contents are mucus. The mucous membrane is moderately hyperemic. The folds in the antrum are not thickened. The gatekeeper is passing through. Duodenal bulb: pink mucous membrane, yellow bile in the lumen. Endoscopic conclusion: superficial gastritis.

Electrocardiography (ECG) from 02.04.2019: sinus tachycardia with a heart rate of 114 beats per minute. The electrical axis of the heart is horizontal (Figure 2).

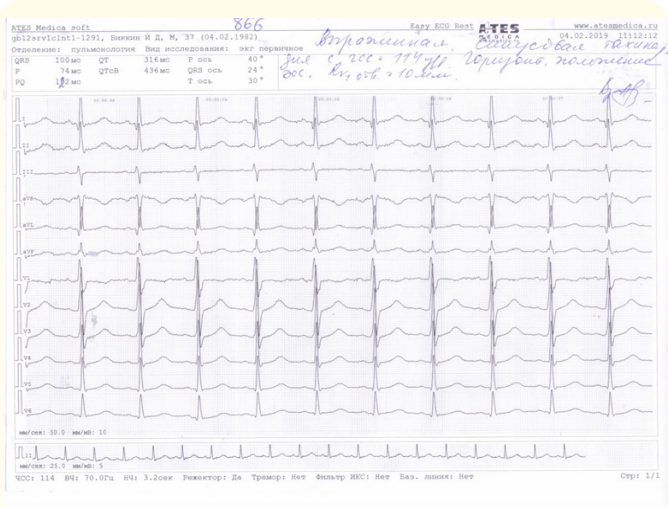

Figure 2: ECG of patient B. 36 years old.

Differential diagnosis

According to complaints, in the emergency room, one could think of dry pleurisy (friction of the visceral and parietal pleural leaves gives pain syndrome, which increases with breathing, coughing and chest movement). However, dry pleurisy rarely occurs with such a high temperature. The complaints are not similar to angina pectoris, osteochondrosis of the thoracic spine and a picture of shingles.

According to the patient's medical history, the picture is similar to dry pleurisy. However, the temperature is too high. He was diagnosed with left-sided pneumonia complicated by pleurisy. The administration of antibiotics did not lead to normalization of temperature. If there was a banal dry pleurisy complicated by pneumonia, the pain on the left should have disappeared against the background of antibacterial and anti-inflammatory therapy. However, the pain on the left did not go away, the temperature did not decrease to normal and, moreover, the picture of the disease wors-

ened. This brought the patient back to the hospital. Thus, there was a discrepancy between the course of the disease and banal pleurisy complicated by pneumonia.

When examining the patient, the discrepancy between the severity of the patient's condition and the physical data for pneumonia and, moreover, for pleurisy is striking. With such a tandem of diseases, there should have been more physical data (the area of bluntness and even dullness (in the presence of fluid in the pleural cavity). In addition, with pneumonia, there should be crepitation, and not small bubbly wheezes.

When examining the abdomen, attention is drawn to its sharp increase due to the huge size of the liver and spleen (Figure 1). As we remember from the patient's life history, hepatitis (of unspecified genesis) was diagnosed for a long time, and then cirrhosis of the liver, which does not fit into these diagnoses. Firstly, what kind of hepatitis from childhood can lead to a real picture? Alcoholic and viral are excluded. Autoimmune hepatitis, which lasts for a long time without treatment, is doubtful. Secondly, all these diseases do not give such a large increase in the liver and spleen. Thirdly, if it is cirrhosis of the liver with such a huge liver and spleen, there should be a picture of cirrhosis of the liver (vascular asterisks, jaundice, ascites, dilation of the veins of the esophagus, etc.). Fourth, why pain in the left half of the abdomen, thrombosis of the splenic vein? But, there is no data for this diagnosis.

From the GBT, we see an increasing leukocytosis, a shift of the formula to the left and an acceleration of RES. This fits into the picture of inflammation. Anemia is increasing, and hemoglobin levels are decreasing.

In the BBT, almost normal ALT indicators are noted, an increase in AST to 3 norms, alkaline phosphatase to 1.5-2 norms, and a slight decrease in the level of PTI. The iron content in the blood is also reduced. Such a BBT cannot be used with a long history of hepatitis and cirrhosis of the liver. There is no increase in bilirubin, slightly decreased PTI, normal fibrinogen levels and practically unchanged GGTP index. Of course, the De-Ritis coefficient is greater than one (this is typical for cirrhosis of the liver), but this diagnosis cannot be made by one indicator.

According to the ultrasound of the AC there is no impression of cirrhosis of the liver. Yes, the liver is huge, but its echogenicity is slightly increased, the echostructure is homogeneous and, most importantly, the portal vein is of normal size and there is no ascites (i.e. there is no portal hypertension). The heterogeneity of the structure of the spleen is noteworthy. This forced us to repeat the ultrasound of the AC.

Repeated ultrasound of the AC in dynamics made it possible to suspect a pathological process in the spleen (suppuration). Ultrasound of the pleural cavity made it possible to exclude pronounced exudative pleurisy.

The absence of varicose veins of the esophagus (VVE) on FGDS, with such large liver and spleen sizes, completely excludes cirrhosis of the liver.

On the ECG (Figure 2) we see sinus tachycardia, a deviation of the electrical axis of the heart (EAH) to the left. Sinus tachycardia is caused by high fever. The EAH is deflected to the left due to the horizontal position of the heart, due to the displacement of the LV to the left by the huge spleen. This is suggested by some other data, namely: if the EAH was deflected to the left due to LV hypertrophy, there would be signs of it on the ECG, namely, the R wave would increase to V6, there would be a deep S in V2-3 and a high R in V6, depression S-T and negative T in V5-6. V1 + V6 or V6 >3.5 mV (Sokolov-Lyon index). In addition, aVL and aVF show that the position is horizontal.

On the X-ray of the chest organs, we see the high standing of the diaphragm on the right and left (Figure 3). Pronounced kyphoscoliosis, displacement of the left ventricle to the left and upward by the large spleen and its compression of the pleura and lung tissue with an auscultative pattern is a symptom of Pena (described in mitral stenosis - an enlarged left atrium presses the lung tissue, causing compression atelectasis of the lung with an auscultative pattern of finely vesicular hirps).

Considering the above, the diagnosis was made: Gaucher disease type 1 (mental underdevelopment, kyphoscoliosis, hepatosplenomegaly, anemia, thrombocytopenia). The threat of rupture of the spleen.

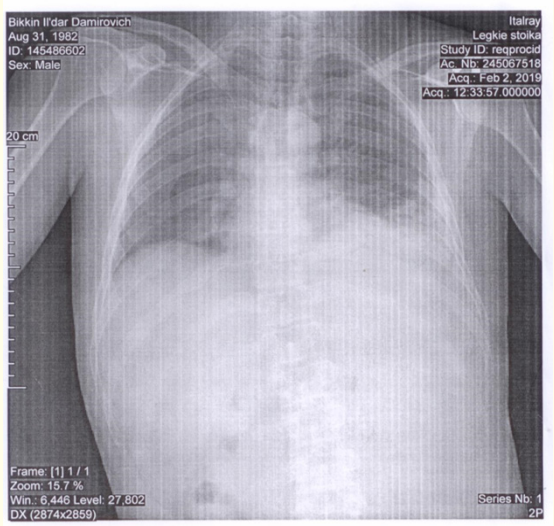

Figure 3: Chest X-ray of patient B. 36 years old.

Due to the increasing threat of rupture of the spleen, due to a purulent abscess (necrosis), the patient was urgently taken for surgery. During surgery: a huge spleen with an abscess.

Morphology (Figure 4). Stained with hematoxylin and eosin. Characteristic changes in Gaucher disease - the cytoplasm of macrophages resembles crumpled tissue paper.

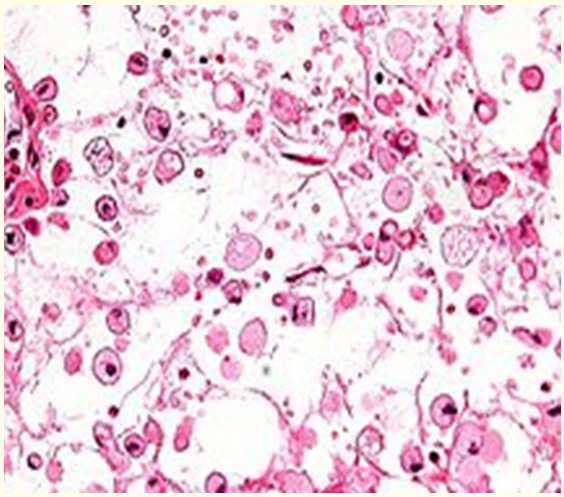

Figure 4

The diagnosis was confirmed by a decrease in the activity of acid beta-glucocerebrosidase in leukocytes and a mutation on the long arm of chromosome 1 (region 1q21q31).

Gaucher disease (ICD10:E.75.2) is the most common form of hereditary fermentopathies, grouped into a group of lysosomal accumulation diseases. The disease is based on a hereditary deficiency in the activity of glucocerebrosidase, a lysosomal enzyme involved in the degradation of cellular metabolism products.

Conclusion

Why was it so long before the correct diagnosis was made? Unfortunately, the lack of clinical thinking has led doctors away from the right line.

Yes, the patient was treated in good faith according to Standards and Clinical recommendations for hepatitis, and then for cirrhosis of the liver. But nothing helped, because the patient had a completely different diagnosis and needed a different treatment that would help the patient. If the patient had been correctly diagnosed at the beginning of the disease (pediatricians, therapists, gastroenterologists) and given the right drug at the time - recombinant glucocerebrosidase, then of course the result would have been completely different.

Conflict of Interest

All authors declare no competing interests.

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